

20 July 2018
[54–18]

Call for submissions – Application A1157

Enzymatic production of Rebaudioside M

FSANZ has assessed an application made by Blue California to amend the *Australia New Zealand Food Standards Code* (the Code) to include a new specification for rebaudioside M (Reb M) produced by an enzymatic conversion method and has prepared a draft food regulatory measure. Pursuant to section 31 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), FSANZ now calls for submissions to assist consideration of the draft food regulatory measure.

For information about making a submission, visit the FSANZ website at [information for submitters](#).

All submissions on applications and proposals will be published on our website. We will not publish material that we accept as confidential, but will record that such information is held. In-confidence submissions may be subject to release under the provisions of the *Freedom of Information Act 1991*. Submissions will be published as soon as possible after the end of the public comment period. Where large numbers of documents are involved, FSANZ will make these available on CD, rather than on the website.

Under section 114 of the FSANZ Act, some information provided to FSANZ cannot be disclosed. More information about the disclosure of confidential commercial information is available on the FSANZ website at [information for submitters](#).

Submissions should be made in writing; be marked clearly with the word ‘Submission’ and quote the correct project number and name. While FSANZ accepts submissions in hard copy to our offices, it is more convenient to receive submissions electronically through the FSANZ website via the link on [documents for public comment](#). You can also email your submission directly to submissions@foodstandards.gov.au.

There is no need to send a hard copy of your submission if you have submitted it by email or via the FSANZ website. FSANZ endeavours to formally acknowledge receipt of submissions within 3 business days.

DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 31 August 2018

Submissions received after this date will not be considered unless an extension had been given before the closing date. Extensions will only be granted due to extraordinary circumstances during the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.

Questions about making submissions or the application process can be sent to standards.management@foodstandards.gov.au.

Hard copy submissions may be sent to one of the following addresses:

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Supporting document

The [following document](#) which informed the assessment of this application is available on the FSANZ website:

SD1 Risk and technical assessment report

Executive summary

Blue California's application seeks permission in the *Australia New Zealand Food Standards Code* (the Code) for a Rebaudioside M (Reb M) produced by a novel production method. That is a multi-step enzymatic conversion process using enzymes sourced from genetically modified strains of *Pichia pastoris*.

The Code permits the use of Reb M and other steviol glycosides as food additives in various food categories subject to prescribed limits and also imposes identity and purity specifications with which Reb M and other steviol glycosides must comply. These current specifications do not allow for Blue California's production method.

Blue California's application seeks an amendment to Schedule 3 - Identity and Purity to include a reference to that production method. This in effect will allow the use of Blue California's Reb M in accordance with the Code's existing permissions and limits for Reb M.

FSANZ's risk assessment - based on the best available scientific evidence – confirmed that neither the Blue California's Reb M nor the enzymes used in the manufacture of that Reb M posed a public health and safety risk. The risk assessment also found that the use of the enzymes in the manufacture of the Reb M in the manner proposed by Blue California (i.e., as a processing aid) is technologically justified.

FSANZ has therefore prepared a draft variation to amend Schedule 3 to include a reference to the production method for Blue California's Reb M in the specifications for Reb M. The draft variation will also amend Schedule 18 to permit the use of the enzymes as processing aids in the manufacture of that Reb M, ensuring compliance with the Code.

The express permission for the enzymes' use as processing aid will also provide the required permission for the enzyme's potential presence in the Reb M as a food produced using gene technology. The enzymes are a food produced using gene technology for Code purposes as they are derived from 'an organism that has been modified using gene technology'.

FSANZ's assessment is that the Blue California Reb M is not itself a food produced using gene technology. The enzymes' use as processing aids in the manufacture of the Reb M does not of itself make the Reb M a genetically modified food for Code purposes. The Reb M itself is not derived from an organism that has been modified using gene technology.

1 Introduction

1.1 The applicant

Blue California is a science-based manufacturer of natural ingredients that are used in food products, beverages, flavours and fragrances, dietary supplements, personal care and cosmetics. They are based in Rancho Santa Margarita, California.

1.2 The application

Blue California's application, accepted on 31 January 2018, seeks permission for a non-traditional production method for a specific form of an intense sweetener food additive, being rebaudioside M (Reb M), which is a specific steviol glycoside. Steviol glycosides are a group of substances permitted as intense sweeteners (food additives) for addition to a variety of foods. The traditional method of production to produce steviol glycosides, including Reb M, uses hot water extraction of the stevia (*S. rebaudiana* Bertoni) leaf, followed by purification and recrystallisation using methanol or ethanol. Conversely, Blue California uses a novel multi-step enzymatic pathway process to manufacture Reb M using the enzymes uridine diphosphate UDP-glucosyltransferase and sucrose synthase. This process facilitates the transfer of glucose to purified stevia leaf extract via glycosidic bonds. The enzymes utilised are sourced from GM strains of *P. pastoris*.

1.3 The current standards

Australian and New Zealand food laws require food for sale to comply with the following requirements of the *Australia New Zealand Food Standards Code* (the Code).

Subsection 1.1.1—10(6) of the Code provides that, unless expressly permitted by the Code, a food for sale cannot contain, as an ingredient or component: a substance 'used as a food additive'; a substance that was 'used as a processing aid'; or a food produced using gene technology'. The Code also imposes identity and purity specifications with which Reb M and other steviol glycosides must comply. Further detail is provided in Appendix 1.

The Code currently permits the use of steviol glycosides as food additives with the INS number 960. They are permitted in a wide range of food categories listed within the table to section S15—5 at maximum permitted levels (MPLs) and at Good Manufacturing Practice (GMP) for tabletop sweeteners only.

However, the current specifications for identity and purity do not allow for Blue California's production method. It should be noted that Blue California is not requesting a change to the purity specification ($\geq 95\%$ steviol glycosides, in paragraph S3—35(4)(b)) or proposing an extension for the use of Reb M in additional food products. Nor do they propose to increase the permitted quantities of Reb M in permitted food products.

1.3.1 International Standards

Steviol glycosides are approved for use in a number of other jurisdictions, including the European Union, Canada, Asia, Central/South America, and Africa (Global Stevia Institute, 2017). In the European Union, commercially available steviol glycoside products must comply with the specifications for steviol glycosides (INS number 960) adopted by the European Commission in 2012 and recently updated in 2016 (EU, 2012, 2016).

1.3.1.1 JECFA

JECFA recently re-evaluated the safety, dietary intake, and specifications for steviol glycosides at its 82nd meeting in 2016. The safety of steviol glycosides as well as the

acceptable daily intake (ADI) of 0 to 4 mg/kg body weight, expressed as steviol, were confirmed. Details of a new manufacturing process for rebaudioside A utilising a strain of *Yarrowia lipolytica* that was genetically modified to overexpress the steviol glycoside biosynthetic pathway were submitted to and reviewed by the Committee. As a result, the Committee issued a new specification monograph for “Rebaudioside A from Multiple Gene Donors Expressed in *Yarrowia lipolytica*” (JECFA, 2016a). The Committee also reviewed data demonstrating the shared metabolism of all steviol glycosides and issued new ‘tentative’ specifications for “Steviol Glycosides from *Stevia rebaudiana* Bertoni” (JECFA, 2016b). These new specifications expanding the definition of steviol glycosides to “a mixture of compounds containing a steviol backbone conjugated to any number or combination of the principal sugar moieties in any of the orientations occurring in the leaves of *Stevia rebaudiana* Bertoni including, glucose, rhamnose, xylose, fructose, and deoxyglucose”. The purity of steviol glycosides from *S. rebaudiana* Bertoni must be no less than 95% total steviol glycosides on the dried basis.

1.3.1.2 USA

A GRAS notification (GRN No. 667) was submitted by Blue California for Reb M produced via enzymatic conversion of purified stevia leaf extract, which is the same product that is the subject of this application. The U.S. FDA responded with no questions to the GRAS status of Blue California’s Reb M produced via conversion for use as a table top sweetener and as a general purpose non-nutritive sweetener in foods.

1.3.1.3 Canada

Health Canada has no objections to the use of Blue California’s high-purity Reb M manufactured using genetically modified yeast, provided that the product is used in accordance with the permitted uses of steviol glycosides as set out in Item S.1.2 of the List of Permitted Sweeteners, is free of yeast cells, and is of food-grade quality.

1.4 Reasons for accepting application

The application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the FSANZ Act; and
- it related to a matter that warranted the variation of a food regulatory measure.

1.5 Procedure for assessment

The application is being assessed under the General Procedure.

2 Summary of the assessment

2.1 Risk assessment

FSANZ has conducted an assessment of the public health and safety risks associated with the Blue California Reb M as a food additive and concluded:

- Recent assessments by FSANZ, Health Canada and JECFA have confirmed that all steviol glycosides undergo the same metabolic pathway to steviol, which is then glucuronidated and excreted in the urine.
- A group Acceptable Daily Intake (ADI), expressed as steviol, is therefore appropriate to cover dietary exposure all steviol glycosides. A small number of genotoxicity studies, studies in laboratory rodents and studies in human volunteers of steviol glycosides have been published since the last assessment by FSANZ (Application A1132, assessment completed in February 2017), but there is no new information that gives reason to change the existing ADI of 0-4 mg/kg bodyweight (bw)/day steviol.
- The Blue California Reb M that is the subject of this application is chemically the same as Reb M extracted directly from *S. rebaudiana* Bertoni and would therefore follow the same metabolic pathway.
- The Blue California Reb M complies with purity specifications of JECFA (JECFA 2016b).
- No major allergens are used to culture the yeast or at any other stage of the production process.
- The source organism, *P. pastoris*, has a long history of industrial use and is commonly used for recombinant gene expression. It is not toxigenic.
- Sufficient information has been provided concerning potential homology between the novel fusion enzymes and known allergens and toxins. There is no evidence of homology sufficient to give rise to concern.

The existing ADI of 0-4 mg/kg bw/day as steviol is appropriate for the Reb M produced using enzymes from genetically modified *P. pastoris* as described in this application. The Blue California Reb M meets the purity specifications listed in S3—35(4).

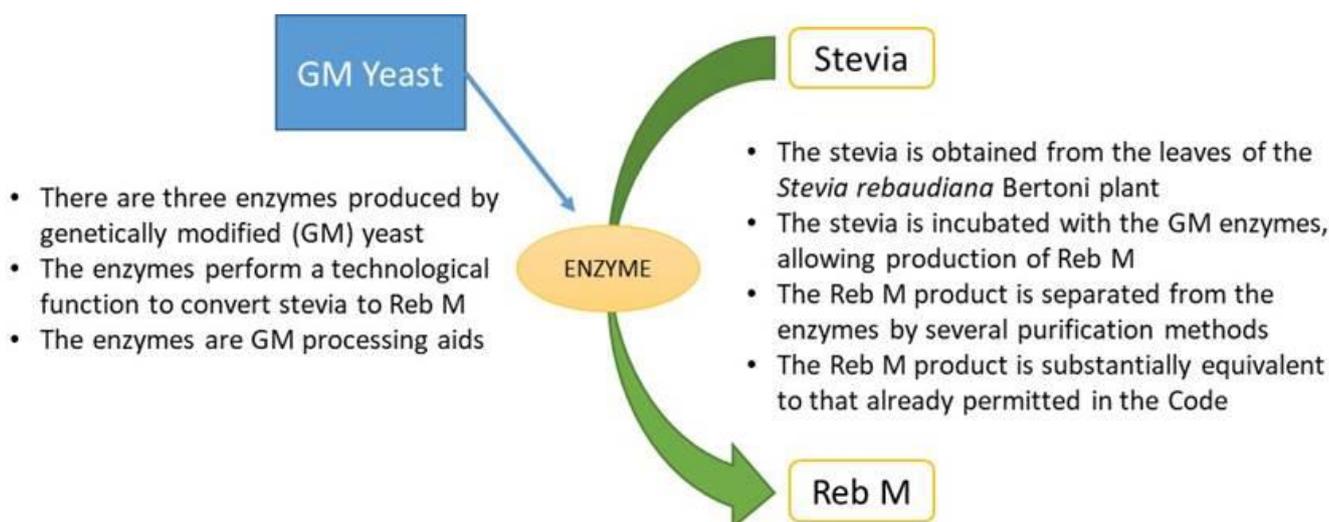
The applicant provided data showing that two yeast production strains have been generated that express three polypeptides, each one being a fusion protein containing a glycosyltransferase and sucrose synthase. Molecular characterisation of the production strains have identified the site of integration for the introduced DNA, confirmed the sequence is as expected and has not undergone any rearrangement, and the introduced DNA is stably inherited. The production strains have also been shown to be genetically stable.

For further details on the risk assessment, refer to the Risk and Technical Assessment Report (SD1).

Production of Blue California Reb M

Blue California's Reb M is derived from steviol glycosides extracted from the *S. rebaudiana* Bertoni plant. This natural plant extract, then undergoes a chemical conversion, driven by enzyme processing aids sourced from GM yeast strains. It is this conversion process which is novel and differs, necessitating a change in the method of manufacture listed in specification S3—35. A schematic of the novel manufacturing process is below in Figure 1.

Figure 1 Conversion of stevia into Reb M via the enzymatic conversion pathway.



Once the Blue California Reb M is extracted from purified stevia leaf extract, it undergoes a multi stage purification process that includes multiple steps to inactivate and remove the enzymes. These steps include heat, treatment with activated carbon, resin purification, and filtration, ensuring the high purity of the Reb M. Blue California has provided assurance through bicinchoninic acid protein testing¹ (BCA assay), that there is no residual protein detected to a level of detection of 5ppm, in its Reb M. It also provided recombinant DNA testing to show that if any rDNA was present it would be at a concentration of <0.1ng/g of Reb M.

FSANZ's assessment of the best scientific evidence available is that it would be very unlikely that any residual enzyme material is present in the final Reb M. Despite this, FSANZ considered it prudent to carry out a safety assessment on the enzymes, noting they are also involved in the new production method for Reb M. The safety assessment confirmed them to be non-toxic and have no homology to known allergens.

2.2 Risk management

The risk management options available to FSANZ, after assessment, were to reject the application or to prepare a draft variation to amend the Code to permit the Blue California's Reb M for use as food additive at levels and in food classes currently permitted in the Code.

On the basis of the risk assessment's conclusion that there are no public health and safety risks, it was considered appropriate to propose to amend Schedule 3 of the Code in order to permit the use of Blue California's Reb M as food additive at the levels and in the foods currently permitted for Reb M in the Code.

An amendment to Schedule 18 is also considered necessary in order to provide regulatory certainty, for the following reasons:

- It is possible, but very unlikely, that Blue California's Reb M may contain miniscule traces of the enzymes that were used in its manufacturing process.

¹ [Bicinchoninic acid \(BCA\) protein assays](#)

- The Code provides that, unless expressly permitted by the Code, a food for sale must not contain, as an ingredient or a component, a substance that was used as a processing aid.
- The use of the enzymes in the manner proposed by the applicant would constitute ‘use as a processing aid’ in the manufacture of the Reb M as a food additive. As mentioned above, the proposed purpose of the specific enzymes had been assessed to comply with the requirements of “used as a processing aid” in section 1.1.2—13 since it performs a specific technological purpose during the production of Blue California’s Reb M and does not perform a technological purpose in the food for sale (i.e., the food additive Reb M).
- As a result, paragraph 1.1.1—10(6)(c) of the Code would require that any residual traces of the enzymes that are present in the Reb M as a component (i.e., as a constituent part of the Reb M) would need to be expressly permitted by the Code.

For these reasons, and to provide regulatory certainty, it is proposed to amend Schedule 18 of the Code to provide an express permission for the enzymes’ use as processing aids in the production of Reb M. It is proposed to list the specific enzymes as processing aids in subsection S18—9(3) for the specific technological purpose of converting purified stevia leaf extract to produce Reb M.

The express permission for the enzymes’ use as processing aids will also provide the permission for the enzyme’s potential presence in the Blue California Reb M as a food produced using gene technology. The enzymes are a food produced using gene technology for Code purposes as they are derived from ‘an organism that has been modified using gene technology’ (i.e., genetically modified yeast). Paragraph 1.1.1—10(6)(g) requires that the presence as an ingredient or component in a food for sale of a food produced using gene technology must be expressly permitted by the Code. Section 1.5.2—3 of Standard 1.5.2 provides that permission for use as a processing aid also constitutes the permission required by paragraph 1.1.1—10(6)(g).

FSANZ’s assessment is that the Blue California Reb M is not itself a food produced using gene technology. The enzymes’ use as processing aids in the manufacture of the Reb M does not of itself make the Reb M a genetically modified food for Code purposes. The Reb M itself is not derived from an organism that has been modified using gene technology. See Figure 1.

2.2.1 Labelling

The Blue California Reb M will be required to be declared as a food additive. Steviol glycosides, including Reb M, are already permitted for use as food additives in the Code.

As a proposed change to the Code from this application is to the specification for Reb M rather than approval of the food additive itself, the labelling requirements relating to steviol glycosides will remain the same, including the requirement in Standard 1.2.4 to declare food additives in the statement of ingredients.

As explained above, FSANZ’s assessment is that Blue California’s Reb M is not itself a food produced using gene technology as, in contrast to the enzyme processing aids used for its manufacture, it is not derived from an organism that has been modified using gene technology. As such, foods for sale that contain Blue California’s Reb M as an ingredient will not be required to be labelled as ‘genetically modified’. Section 1.5.2—4 requires certain foods for sale that consist of or have as an ingredient, food that is a genetically modified food to be labelled as ‘genetically modified’. FSANZ also notes that the Code’s labelling requirements – including those imposed by section 1.5.2—4 – generally apply only to foods

for retail sale and to foods sold to a caterer under subsection 1.2.1—8(1) and section 1.2.1—15 respectively. It is understood that Blue California's Reb M itself would not be sold for retail sale or to a caterer because it is a highly concentrated intense sweetener.

In terms of the enzymes used as processing aids to manufacture Blue California's Reb M, the Code exempts processing aids (which include a number of permitted enzymes as listed in Schedule 18) from the requirement to be declared in the statement of ingredients. FSANZ's understanding is that this exemption will apply in this case.

FSANZ also notes that the enzymes used as processing aids to manufacture Blue California's Reb M are very unlikely to be present as an ingredient in a food for sale which contains Reb M (See section 2.2 above). If so, the requirement to label as 'genetically modified' would not apply to that food for sale because the labelling requirements only apply to food that consists of, or has as an ingredient, a genetically modified food (section 1.5.2—4(1)).

2.2.2 Risk management conclusion

Taking account of the risk assessment conclusions in (section 2.1), the risk management considerations (section 2.2) along with the benefits to industry and consumers (section 2.4.1.1), the risk management conclusion is to permit the use as a food additive of Blue California's Reb M, manufactured using this novel enzymatic production method.

To provide that permission, section S3—35 of Schedule 3 of the Code will be amended to refer to the specific manufacturing method for Blue California's Reb M.

The permitted technological purpose of Blue California's Reb M's use as a food additive is that of an intense sweetener and will be permitted in Schedule 15, at the current MPLs and specified food classes and at GMP levels for tabletop sweeteners for steviol glycosides. It will similarly utilise the current INS number 960.

The enzymes used to produce Reb M will also be listed as enzymatic processing aids in subsection S18—(9)(3). Permission for these enzyme processing aids will be limited to the specific purpose of producing Reb M from purified stevia leaf extract only.

2.3 Risk communication

2.3.1 Consultation

Consultation is a key part of FSANZ's standards development process. FSANZ developed and applied a basic communication strategy to this application. All calls for submissions are notified via the Food Standards Notification Circular, media release, FSANZ's social media tools and Food Standards News.

The process by which FSANZ considers standard development matters is open, accountable, consultative and transparent. Public submissions are called to obtain the views of interested parties on issues raised by the application and the impacts of regulatory options. FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application.

The draft variation will be considered for approval by the FSANZ Board taking into account public comments received from this call for submissions.

2.3.2 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obliged

to notify WTO members where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

There are relevant international standards for Reb M. Amending the Code to permit Reb M produced by an enzymatic conversion method is unlikely to have a significant effect on international trade as the specification is identical to currently permitted Reb M's which use the traditional hot water extraction method. Therefore, a notification to the WTO under Australia's and New Zealand's obligations under the WTO Technical Barriers to Trade or application of Sanitary and Phytosanitary Measures Agreement was not considered necessary.

2.4 FSANZ Act assessment requirements

When assessing this application and the subsequent development of a food regulatory measure, FSANZ has had regard to the following matters in section 29 of the FSANZ Act:

2.4.1 Section 29

2.4.1.1 Cost benefit analysis

Objectives for cost benefit consideration

The objective of this consideration is to determine whether consumers, industry and government are likely to benefit from a change to the status quo by accepting the application.

Accepting the application would mean varying Schedule 3 to permit the use of Reb M produced by an enzymatic conversion method as a food additive in certain foods. As FSANZ can prepare a draft variation or reject the application under section 30 of the FSANZ Act, preparing a draft variation to permit Blue California's Reb M is the only proposed measure that has been considered against the status quo (i.e. rejecting the application).

FSANZ can conclude there is no other practical food regulatory measure aside from accepting or remaining with the status quo (i.e. rejecting the application).

Standing exemption from FSANZ completing a regulatory impact statement

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the approval of additional processing aids (OBPR correspondence dated 24 November 2010, reference 12065). This standing exemption was provided as permitting additional processing aids is a minor, deregulatory change and their use is voluntary. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

Despite that exemption, the FSANZ Act requires FSANZ to consider whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the consumers, government or industry (section 29(2)(a)).

Costs and benefits

The consideration of the costs and benefits is not intended to be an exhaustive, quantitative economic analysis of the proposed measures. The considerations/assessment sought to highlight the likely benefits and costs of changing from the status quo by accepting the application.

Table 1 Proposed food regulatory measure – accept the application

Sector	Costs or benefits to sector
Consumers	<p>The use of Blue California’s Reb M as a food additive in the manner proposed will not pose a health or safety risk for consumers. The benefits to the consumer would mirror those for other steviol glycosides currently permitted for use in Australia and New Zealand. Blue California’s Reb M, like other steviol glycosides, would be used in foods and beverages to replace sugar, which will benefit consumers seeking products that have reduced sugar and/or energy content. In addition, this would also include consumers with specific medical conditions that require reduced sugar intake, such as those with diabetes, as the consumption of steviol glycosides does not interfere with glucose homeostasis (EFSA, 2010).</p> <p>Consumers may also benefit from the choice of additional (and better quality) food products that become available due to the use of this Reb M by Australian and New Zealand manufacturers and access to products manufactured using enzyme that are currently manufactured overseas.</p>
Industry	<p>Along with other Reb M’s, Blue California’s Reb M has more favourable sensory characteristics when compared to the major glycosides (i.e., stevioside, rebaudioside A) and has taste profiles more reflective of sucrose. Hence the development of the new technology to produce a glycoside with preferential sensory characteristics for product development can provide a benefit in terms of product and/or competitive advantage to food manufacturers.</p> <p>In the U.S., Blue California’s Reb M produced via enzymatic conversion of purified stevia leaf extract has GRAS status for use as a table top sweetener and a general purpose non-nutritive sweetener in foods. Permission to use Blue California’s Reb M as a food additive, will enable Australia/New Zealand food manufacturers to access and use a product assessed as safe that is available to their overseas competitors. This will improve their capacity to compete in overseas markets. Use by industry is voluntary, therefore it will only be used where industry believe a net benefit exists above using existing intense sweeteners.</p>
Governments	<p>Since Blue California does not intend to propose an extension for the use of Reb M in additional food products nor do it wish to propose to increase the permitted quantities of Reb M in permitted food products, there is no perceived benefit or added cost to governments.</p>

Conclusions from cost benefit considerations

The direct and indirect benefits that would arise from permitting the use of this particular Reb M as a food additive will most likely outweigh the costs arising from that permission being granted.

2.4.1.2 Other measures

FSANZ considers that there are no other measures (whether available to FSANZ or not) that would be more cost-effective than a food regulatory measure developed as a result of this application.

2.4.1.3 Any relevant New Zealand standards

The Standards and Schedules relevant to the draft variation apply in both Australia and New Zealand. There are no relevant New Zealand only Standards.

2.4.1.4 Any other relevant matters

Other relevant matters are considered below.

2.4.2. Subsection 18(1)

FSANZ has also considered the three objectives in subsection 18(1) of the FSANZ Act during the assessment.

2.4.2.1 Protection of public health and safety

FSANZ concluded that there are no safety concerns associated with Blue California's Reb M produced using enzymes from genetically modified *P. pastoris*. For more detail, see SD1.

2.4.2.2 The provision of adequate information relating to food to enable consumers to make informed choices

The generic labelling requirements will apply to the use of *Reb M* in food (see Section 2.2.2 above).

2.4.2.3 The prevention of misleading or deceptive conduct

No issues have been identified with this application relevant to this objective.

2.4.3 Subsection 18(2) considerations

FSANZ has also had regard to:

- **the need for standards to be based on risk analysis using the best available scientific evidence**

FSANZ used the best available scientific evidence to conduct the risk assessment which is provided in SD1. The applicant submitted a dossier of scientific studies as part of its application. Other technical information including scientific literature was also used in assessing the application.

- **the promotion of consistency between domestic and international food standards**

The Blue California Reb M specifications are identical to those established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2006) and the Food Chemicals Codex (Food Chemicals Codex, 2015).

Blue California's Reb M is permitted for use in the USA and Canada.

- **the desirability of an efficient and internationally competitive food industry**

Permission to use this particular Reb M as a food additive will enable Australia/New Zealand food manufacturers to access and use a product assessed as safe that is available to some overseas competitors. This will improve their capacity to compete in overseas markets. See discussion at Section 2.4.1 above.

- **the promotion of fair trading in food**

The Blue California Reb M has been assessed as safe and is permitted for use the USA and Canada. It is therefore appropriate that Australian and New Zealand food industries can also benefit by gaining permission to use this same enzyme preparation.

- **any written policy guidelines formulated by the Ministerial Council²**

The Policy Guideline 'Addition to Food of Substances other than Vitamins and Minerals'³ includes specific order policy principles for substances added to achieve a solely technological function, such as food additives. These specific order policy principles state that permission should be granted where:

- the purpose for adding the substance can be articulated clearly by the manufacturer as achieving a solely technological function (i.e. the 'stated purpose')
- the addition of the substance to food is safe for human consumption
- the amounts added are consistent with achieving the technological function
- the substance is added in a quantity and a form which is consistent with delivering the stated purpose
- no nutrition, health or related claims are to be made in regard to the substance.

FSANZ has determined that permitting Blue California's Reb M produced by an enzymatic conversion method, is consistent with these specific order policy principles.

3 Draft variation

The draft variation to the Code is at Attachment A and is intended to take effect on gazettal.

A draft explanatory statement is at Attachment B. An explanatory statement is required to accompany an instrument if it is lodged on the Federal Register of Legislation.

² Now known as the Australia and New Zealand Ministerial Forum on Food Regulation (convening as the Australia and New Zealand Food Regulation Ministerial Council)

³ [Foodstandards policy pages](#)

4 References

[Global Stevia Institute 2017](#) Accessed 1 Jun 2018

[GRAS Notice \(GRN\) No. 667](#) Blue California Reb M produced via conversion for use as a table top sweetener and as a general purpose non-nutritive sweetener in foods. Accessed 1 Jun 2018

[COMMISSION REGULATION \(EU\) No 231/2012 of 9 March 2012](#) laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. Accessed 1 Jun 2018

[COMMISSION REGULATION \(EU\) 2016/1814 of 13 October 2016](#) amending the Annex to Regulation (EU) No 231/2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards specifications for steviol glycosides (E 960). Accessed 1 Jun 2018

[JECFA \(2016a\)](#). Rebaudioside A from multiple gene donors expressed in *Yarrowia lipolytica* [Prepared at the 82nd JECFA, 2016]. In: *Combined compendium of food additive specifications*. 82nd Meeting, June 7-16, Geneva, Switz. (FAO JECFA Monographs 19). Rome, Italy: Food and Agriculture Organization of the United Nations (FAO) / Geneva, Switz.: World Health Organization (WHO), pp. 91-95. Accessed 1 Jun 2018

[JECFA \(2016b\)](#). Steviol glycosides from *Stevia rebaudiana* Bertoni (tentative) [New specifications prepared at the 82nd JECFA, 2016), Superseding specifications prepared at the 73rd JECFA (2010)]. In: *Compendium of Food Additive Specifications*. 82nd Meeting, June 7-16, Geneva, Switz. (FAO JECFA Monographs 19). Rome, Italy: Food and Agriculture Organization of the United Nations (FAO) / Geneva, Switz.: World Health Organization (WHO), pp. 106-111. Accessed 1 Jun 2018.

Attachments

- A. Draft variation to the *Australia New Zealand Food Standards Code*
- B. Draft Explanatory Statement

Attachment A – Draft variation to the Australia New Zealand Food Standards Code



Food Standards (Application A1157 – Enzymatic production of Rebaudioside M) Variation

The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by the Delegate]

[Insert Name and Position of Delegate]

Delegate of the Board of Food Standards Australia New Zealand

Note:

This variation will be published in the Commonwealth of Australia Gazette No. FSC **XX on XX Month 20XX**. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

1 Name

This instrument is the *Food Standards (Application A1157 – Enzymatic production of Rebaudioside M) Variation*.

2 Variation to standards in the *Australia New Zealand Food Standards Code*

The Schedule varies Standards in the *Australia New Zealand Food Standards Code*.

3 Commencement

The variation commences on the date of gazettal.

Schedule

[1] Schedule 3 is varied by omitting subsection S3—35(2), substituting

- (2) The preparation must be obtained from the leaves of the *Stevia rebaudiana* Bertoni plant by using one of the following processes:
 - (a) the leaves are extracted with hot water and the extracts are purified using ion-exchange resins followed by recrystallisation from methanol or aqueous ethanol;
 - (b) by enzymatic conversion of purified stevia leaf extract to produce rebaudioside M using protein engineered enzymes that:
 - (i) contain both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and
 - (ii) are sourced from *Pichia pastoris* strain UGT-A, UGT-B1 or UGT-B2.
- (2A) The final product may be spray dried.

[2] Schedule 18 is varied by inserting in the table to subsection S18—9(3), in alphabetical order

Protein engineered enzymes that: contain both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and are sourced from <i>Pichia pastoris</i> strain UGT-A, UGT-B1 or UGT-B2	For the conversion of purified stevia leaf extract to produce rebaudioside M	GMP
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Attachment B – Draft Explanatory Statement

1. Authority

Section 13 of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) provides that the functions of Food Standards Australia New Zealand (the Authority) include the development of standards and variations of standards for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

Division 1 of Part 3 of the FSANZ Act specifies that the Authority may accept applications for the development or variation of food regulatory measures, including standards. This Division also stipulates the procedure for considering an application for the development or variation of food regulatory measures.

FSANZ accepted application A1157 which sought an amendment to Schedule 3 of the Code to prescribe a new specification for rebaudioside M (Reb M) produced by a particular enzymatic conversion method.

The Authority considered the application in accordance with Division 1 of Part 3 of the FSANZ Act and has prepared a draft variation.

2. Purpose

The Authority has prepared a draft variation to amend subsection S3—35(2) of Schedule 3 of the Code. The amendment will include in the specification provided by that subsection a reference to the enzymatic conversion method used to produce the Blue California's Reb M. The amendment's effect would be to permit Reb M produced by that method to be used as a food additive in accordance with the existing permissions and limits for steviol glycosides (including containing Reb M) in the Code

The Authority has also prepared a draft variation to amend Schedule 18 of the Code to permit the use of the specific enzymes as processing aids in the processing of the Blue California's Reb M in accordance with Standard 1.3.3 of the Code.

3. Documents incorporated by reference

The variations to food regulatory measures do not incorporate any documents by reference.

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of application A1157 will include one round of public consultation following an assessment and the preparation of a draft Standard and associated assessment summary.

A Regulation Impact Statement was not required because the proposed variations to Schedule 3 are likely to have a minor impact on business and individuals.

5. Statement of compatibility with human rights

This instrument is exempt from the requirements for a statement of compatibility with human rights as it is a non-disallowable instrument under section 94 of the FSANZ Act.

6. Variation

Item [1]

Item [1] amends Schedule 3 of the Code. The item omits S3—35(2) and substitutes new subsection S3—35(2) and (2A).

The new subsection S3—35(2) includes a reference to the enzymatic conversion of purified stevia leaf extract to produce Reb M using protein engineered enzymes that: contain both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and are sourced from *Pichia pastoris* strain UGT-A, UGT-B1 or UGT-B2.

The new subsection S3—35(2A) restates the proviso in the current subsection S3—35(2) that the final product may be spray dried.

The effect of this amendment is to permit Reb M produced using this method to be used as a food additive in accordance with the existing food additive permissions in the Code for steviol glycosides (including containing Reb M).

Item [2]

Item [2] amends Schedule 18. The item inserts a new entry into the table to subsection S18—9(3). The effect of the new entry would be to permit the use of specific enzymes as a processing aid in the manufacture of Reb M for the following technological purpose: the conversion of purified stevia leaf extract to produce Reb M. The permitted enzymes are protein engineered enzymes that: contain both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and are sourced from *Pichia pastoris* strain UGT-A, UGT-B1 or UGT-B2. The permission includes the condition that the maximum permitted amount used as a processing aid must be consistent with Good Manufacturing Practice (as defined by section 1.1.2—2(3) of the Code).

APPENDIX 1

Food additives

Section 1.3.1—3 of the Code details which substances are permitted to be used as a food additive for the purposes of the Code. The permitted food additives for different food categories are listed in the table to section S15—5 of the Code.

Section 1.1.2—11 also provides that a substance is ‘used as a food additive’ if it is added to a food to perform one or more technological functions listed in schedule 14 of the Code and is one of a number of substances listed in that section. These include a substance identified in the table to section S15—5 as permitted food additive.

Schedule 14 lists the permitted technological purposes of food additives. The table in section S14—2 of that schedule provides that use as an intense sweetener is a permitted purpose.

Schedules 15 and 16 list the specific food additive permissions for different categories of food products.

Processing aids

Paragraph 1.1.1—10(6)(c) provides that a food for sale must not have, as an ingredient or a component, a substance that is used as a processing aid, unless expressly permitted.

Standard 1.3.3 and Schedule 18 list the permitted processing aids. The table to subsection S18—9(3) lists those substances, including enzymes, that are permitted to be used as processing aids for specific technological purposes.

Section 1.1.2—13 defines the expression ‘used as a processing aid.’ That definition imposes requirements on substances permitted by Standard 1.3.3 and Schedule 18 to be used as a processing aid, such that it does not perform a technological purpose in the final food for sale.

Enzymes used in food manufacturing and/or processing are considered processing aids as although they may be present in the final food, they no longer provide a technological purpose in the final food.

Labelling

Paragraph 1.1.1—10(8) of the Code provides that food for sale must comply with all relevant labelling requirements imposed by the Code for that food.

In general, the Code’s labelling requirements apply only to foods for retail sale and to foods sold to a caterer under subsection 1.2.1—8(1) and section 1.2.1—15 respectively.

Standard 1.2.4 of the Code generally requires food products to be labelled with a statement of ingredients. Subsection 1.2.4—7(1) of that Standard requires food additives to be declared in the statement of ingredients.

Schedule 8 (for statement of ingredients) lists the names and code numbers of food additives that are to be used for labelling purposes. Schedule 8 refers to steviol glycosides (INS code number 960) which is currently permitted to be added to food as a food additive.

Processing aids are generally exempt from the requirement to be declared in the statement of ingredients. See paragraphs 1.2.4—3(2)(d) and (e) in Standard 1.2.4.

Section 1.5.2—4 of Standard 1.5.2 outlines requirements for labelling of certain foods for sale that consist of or have as an ingredient, food that is a genetically modified food. A *genetically modified food* is defined in subsection 1.5.2—4(5) as a *food produced using gene technology* that contains novel DNA or novel protein or is listed in section S26—3.

Identity and purity requirements

Paragraph 1.1.1—15(1)(a) of the Code requires substances used as food additives to comply with any relevant identity and purity specifications listed in Schedule 3 of the Code.

Sections S3—31 and S3—32 of Schedule 3 provide specifications for Reb M and for steviol glycoside mixtures containing Reb M. These refer to primary source specifications for steviol glycosides contained within section S3—2, being either S3—2(1)(b) [the FAO JECFA Monograph], S3-2(1)(c) [the Food Chemicals Codex] or S3—2(1)(d) [European Commission Regulation No 231/2012 (EU, 2012) laying down specifications for food additives]. Specifications for steviol glycosides from these primary sources, including Reb M, include a method of production where the substance is extracted from the leaves of stevia (*S. rebaudiana* Bertoni).

Section S3—35 of Schedule 3 provides a specification for steviol glycosides prepared from the leaves of stevia (*S. rebaudiana* Bertoni), including Reb M. The specification permits only one method of production, namely extraction using the traditional hot water extraction method. The Blue California Reb M does not comply with this specification due to its different method of production.